

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

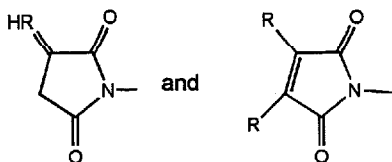
1. (currently amended): A composition comprising a block copolymer having an overall ionic charge and associated with the polymer a biologically active compound having a charge opposite that of the polymer and is characterised in that block copolymer comprises at least one zwitterionic block which has pendant zwitterionic groups and at least one ionic block which comprise ionic groups to confer said overall ionic charge, wherein the biologically active compound and polymer are associated with one another in the form of particles.
2. (previously presented): A composition according to claim 1 in which the biologically active compound is anionic.
3. (previously presented): A composition according to claim 2 in which the active compound is a nucleic acid.
4. (previously presented): A composition according to claim 3 in which the nucleic acid is selected from the group consisting of oligo nucleotides, having 5 to 80 bases, single stranded RNA, single stranded DNA and double stranded DNA.
5. (original): A composition according to claim 1 in which the biologically active compound is an anionic drug.
6. (previously presented): A composition according to claim 1 in which the biologically active compound and polymer are associated with one another in the form of particles having an average diameter less than 200 μm .

7. (original): A composition according to claim 6 which is an aqueous composition in which the particles are suspended.

8. (previously presented): A composition according to claim 1 in which the zwitterionic block is formed from ethylenically unsaturated monomers including a zwitterionic monomer having the general formula



in which Y is an ethylenically unsaturated group selected from the group consisting of $\text{H}_2\text{C}=\text{CR}-\text{CO}-\text{A}-$, $\text{H}_2\text{C}=\text{CR}-\text{C}_6\text{H}_4-\text{A}^1-$, $\text{H}_2\text{C}=\text{CR}-\text{CH}_2\text{A}^2$, $\text{R}^2\text{O}-\text{CO}-\text{CR}=\text{CR}-\text{CO}-\text{O}$, $\text{RCH}=\text{CH}-\text{CO}-\text{O}-$, $\text{RCH}=\text{C}(\text{COOR}^2)\text{CH}_2-\text{CO}-\text{O}$,



A is $-\text{O}-$ or NR^1 ;

A^1 is selected from the group consisting of a bond, $(\text{CH}_2)_l\text{A}^2$ and $(\text{CH}_2)_l\text{SO}_3^-$ in which l is 1 to 12;

A^2 is selected from the group consisting of a bond, $-\text{O}-$, $\text{O}-\text{CO}-$, $\text{CO}-\text{O}$, $\text{CO}-\text{NR}^1-$, $-\text{NR}^1-\text{CO}$, $\text{O}-\text{CO}-\text{NR}^1-$, and $\text{NR}^1-\text{CO}-\text{O}-$;

R is hydrogen or C_{1-4} alkyl;

R^1 is hydrogen, C_{1-4} alkyl or BX ;

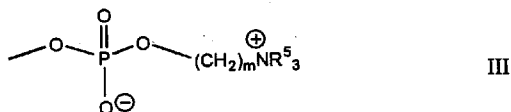
R^2 is hydrogen or C_{1-4} alkyl;

B is selected from the group consisting of a bond, straight and branched alkanediyl groups, alkylene oxaalkylene groups, and alkylene (oligooxalkylene) groups, optionally containing one or more fluorine substituents; and

X is a zwitterionic group.

9. (previously presented): A composition according to claim 8 in which X comprises a cation selected from the group consisting of ammonium, phosphonium and sulphonium groups

10. (previously presented): A composition according to claim 8 in which X has the general formula III



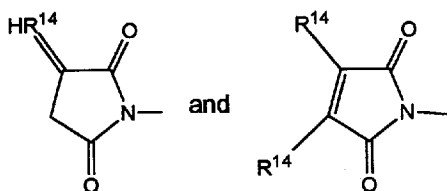
11. (previously presented): A composition according to claim 8 in which the ethylenic unsaturated group Y is $\text{H}_2\text{C}=\text{CR}-\text{CO}-\text{A}-$, in which R is hydrogen or methyl and A is NH or O.

12. (previously presented): A composition according to claim 8 in which the zwitterionic monomer is 2-methacryloyloxyethyl-2'-trimethylammonium ethyl phosphate inner salt.

13. (previously presented): A composition according to claim 1 in which the ionic block is formed of ethylenically unsaturated monomers including an ionic monomer of general formula VI



in which Y¹ is selected from the group consisting of H₂C=CR¹⁴-CO-A⁸-, H₂C=CR¹⁴-C₆H₄-A⁹-, H₂C=CR¹⁴-CH₂A¹⁰-, R¹⁶O-CO-CR¹⁴=CR¹⁴-CO-O-, R¹⁴CH=CH-CO-O-, R¹⁴CH=C(COOR¹⁶)CH₂-CO-O-,



A⁸ is -O- or NR¹⁵;

A⁹ is selected from the group consisting of a bond, (CH₂)_qA¹⁰ and (CH₂)_qSO₃- in which q is 1 to 12;

A¹⁰ is selected from the group consisting of a bond, -O-, O-CO-, CO-O, CO-NR¹⁵-, -NR¹⁵-CO, O-CO-NR¹⁵, and NR¹⁵-CO-O-;

R¹⁴ is hydrogen or C₁₋₄ alkyl;

R¹⁵ is hydrogen, C₁₋₄ alkyl or B¹Q;

R¹⁶ is hydrogen or C₁₋₄ alkyl;

B¹ is selected from the group consisting of a bond, straight and branched alkanediyl groups, alkylene oxaalkylene groups and alkylene (oligooxalkylene) groups, optionally containing one or more fluorine substituents; and

Q is an ionic or ionisable moiety.

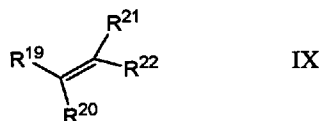
14. (previously presented): A composition according to claim 13 in which Q is selected from groups having the formula -NR¹⁷_p, -PR¹⁷_p and SR¹⁷_r, in which p is 2 or 3, r is 1 or 2, the groups R¹⁷ are the same or different and each is selected from the group consisting of hydrogen, C₁₋₂₄ alkyl and aryl, or two of the groups R¹⁷ together with the heteroatom to which they are attached from a 5 to 7 membered heterocyclic ring or three R¹⁷ groups together with the heteroatom to which they are attached form a 5 to 7 membered heteroaromatic ring, either of which rings may be fused to another 5 to 7 membered saturated or unsaturated ring, and any of the R¹⁷ groups may be substituted by amino or hydroxyl groups or halogen atoms.

15. (previously presented): A composition according to claim 14 in which Q is -NR¹⁷₂ where each R¹⁷ is the same and is C₁₋₁₂-alkyl.

16. (previously presented): A composition according to claim 13 in which B¹ is a C₂₋₆-alkanediyl.

17. (previously presented): A composition according to claim 8 in which the ethylenically unsaturated monomers include comonomer.

18. (currently amended): A composition according to claim 17 in which the comonomer has the general formula IX



in which R¹⁹ is selected from the group consisting of hydrogen, halogen, C₁₋₄ alkyl and groups COOR²³ in which R²³ is hydrogen and C₁₋₄ alkyl;

R²⁰ is selected from the group consisting of hydrogen, halogen and C₁₋₄ alkyl;

R²¹ is selected from the group consisting of hydrogen, halogen, C₁₋₄ alkyl and groups COOR²³ provided that R¹⁹ and R²¹ are not both COOR²³; and

R²² is selected from the group consisting of C₁₋₁₀ alkyl, a C₁₋₂₀ alkoxy carbonyl, a mono- or di-(C₁₋₂₀ alkyl) amino carbonyl, a C₆₋₂₀ aryl, C₇₋₂₀ aralkyl, C₆₋₂₀ aryloxy carbonyl, C₁₋₂₀-aralkyloxy carbonyl, C₆₋₂₀ arylamino carbonyl, C₇₋₂₀ aralkyl-amino, hydroxyl and C₂₋₁₀ acyloxy groups, any of which may have one or more substituents selected from the group consisting of halogen atoms, alkoxy, oligo-alkoxy, aryloxy, acyloxy, acylamino, amine, carboxyl, sulphonyl, phosphoryl, phosphino, zwitterionic, hydroxyl, vinyloxy carbonyl, and reactive silyl and silyloxy groups;

or R²² and R²¹ or R²² and R²⁰ may together form -CONR²⁴CO in which R²⁴ is a C₁₋₂₀ alkyl group.

19. (previously presented): A composition according to claim 1 in which at least one of the blocks has a polydispersity of molecular weight less than 2.0.

20. (previously presented): A composition according to claim 1 in which the degree of polymerisation of the ionic block is in the range 5 to 2000 and the degree of polymerisation of the zwitterionic block is in the range 2 to 1000 and in which the ratio of the degrees of polymerisation of the ionic block to the zwitterionic block is in the range 1:5 to 10:1.

21. (previously presented): A composition according to claim 1 in which at least one of the blocks is formed by a living radical polymerisation process.

22. (previously presented): A composition according to claim 1 in which the relative amounts of biologically active compound and polymer are in the range 1:5 to 10:1 based on equivalents of the polymer to active compound charged groups.

23. (withdrawn): Process for producing a composition according to claim 1 in which an aqueous dispersion of a block copolymer having an overall ionic charge and comprising at least one zwitterionic block which has pendant zwitterionic groups and at least one zwitterionic block which comprise ionic groups to confer said overall ionic charge, is contacted with a biologically active compound having a charge opposite that of the block copolymer, to form an aqueous suspension of block copolymer and associated active.

24. (withdrawn): Process according to claim 23 in which the average particle size of the suspension is less than 200nm.

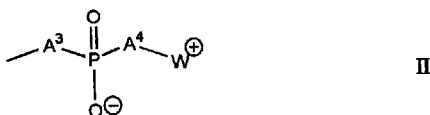
25. (withdrawn): Process according to claim 23 in which the ratio of equivalents of ionic groups in the block copolymer to ionic groups in the biologically active compound is in the range 10:1 to 1:5.

26. (withdrawn): A process according to claim 23 in which the biologically active is in solution form in an aqueous vehicle when it is contacted with the block copolymer dispersion.

27. (canceled).

28. (previously presented): A composition according to claim 2 in which the biologically active compound is polyanionic.

29. (previously presented): A composition according to claim 9 in which X has the general formula II



in which the moieties A^3 and A^4 , which are the same or different, are -O-, -S-, -NH- or a valence bond and W^+ is a group comprising an ammonium, phosphonium or sulphonium cationic group and a group linking the anionic and cationic moieties which is a C_{1-12} alkanediyl group.

30. (previously presented): A composition according to claim 29 in which W^+ is a group of formula

$-W^1-N^+R^3_3$, $-W^1-P^+R^4_3$, $-W^1-S^+R^4_2$ or $-W^1\text{-Het}^+$ in which:

W^1 is selected from the group consisting of alkanediyl of 2-6 carbon atoms optionally containing one or more ethylenically unsaturated double or triple bonds, disubstituted-aryl (arylene), alkylene arylene, arylene alkylene, and alkylene aryl alkylene, cycloalkanediyl, alkylene cycloalkyl, cycloalkyl alkylene or alkylene cycloalkyl alkylene, which group W^1 optionally contains one or more fluorine substituents and/or one or more functional groups; and
either the groups R^3 are the same or different and each is selected from the group consisting of hydrogen, alkyl of 1 to 4 carbon atoms, and aryl or two of the groups R^3 together

with the nitrogen atom to which they are attached form an aliphatic heterocyclic ring containing from 5 to 7 atoms, or

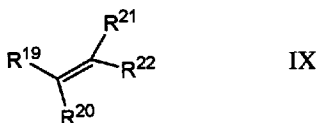
the three groups R^3 together with the nitrogen atom to which they are attached as heteroaromatic ring having 5 to 7 atoms, either of which rings may be fused with another saturated or unsaturated ring to form a fused ring structure containing from 5 to 7 atoms in each ring, and optionally one or more of the groups R^3 is substituted by a hydrophilic functional group, and

the groups R^4 are the same or different and each is R^3 or a group OR^3 , where R^3 is as defined above; and

Het is an aromatic nitrogen-, phosphorus- or sulphur-containing ring.

31. (previously presented): A composition according to claim 13 in which the ethylenically unsaturated monomers include a comonomer.

32. (previously presented): A composition according to claim 31 in which the comonomer has the general formula IX



in which R^{19} is selected from the group consisting of hydrogen, halogen, C_{1-4} alkyl and groups $COOR^{23}$ in which R^{23} is hydrogen or C_{1-4} alkyl;

R^{20} is selected from the group consisting of hydrogen, halogen and C_{1-4} alkyl;

R^{21} is selected from the group consisting of hydrogen, halogen, C_{1-4} alkyl and groups $COOR^{23}$ provided that R^{19} and R^{21} are not both $COOR^{23}$; and

R^{22} is selected from the group consisting of C_{1-10} alkyl, a C_{1-20} alkoxy carbonyl, mono- and di-(C_{1-20} alkyl) amino carbonyl, C_{6-20} aryl, C_{7-20} aralkyl, C_{6-20} aryloxy carbonyl, C_{1-20} -aralkyloxy carbonyl, C_{6-20} arylamino carbonyl, C_{7-20} aralkyl-amino, hydroxyl and C_{2-10} acyloxy groups, any of which may have one or more substituents selected from the group consisting of halogen atoms, alkoxy, oligo-alkoxy, aryloxy, acyloxy, acylamino, amine, carboxyl, sulphonyl, phosphoryl, phosphino, zwitterionic, hydroxyl, vinyloxy carbonyl and reactive silyl and silyloxy groups;

or R^{22} and R^{21} or R^{22} and R^{20} may together form $-CONR^{24}CO$ in which R^{24} is a C_{1-20} alkyl group.

33. (previously presented): A composition according to claim 20 in which the degree of polymerisation of the ionic block is in the range 10 to 250, the degree of polymerisation of the zwitterionic block is in the range 5 to 100 and the ratio of the degrees of polymerisation of the ionic block to the zwitterionic block is in the range 1:1 to 5:1.

34. (previously presented): A composition according to claim 21 in which the living radical polymerisation process is a group or atom transfer polymerisation process.

35. (previously presented): A composition according to claim 22 in which the said relative amounts are in the range 1:2 to 5:2.

36. (withdrawn): A process according to claim 23 in which the biologically active compound is anionic.

37. (withdrawn): A process according to claim 36 in which the biologically active compound is polyanionic.

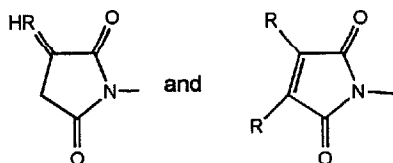
38. (withdrawn): A process according to claim 36 in which the active compound is a nucleic acid.

39. (withdrawn): A process according to claim 38 in which the nucleic acid is selected from the group consisting of oligo nucleotides, having 5 to 80 bases, single stranded RNA, single stranded DNA and double stranded DNA.

40. (withdrawn): A process according to claim 23 in which the zwitterionic block is formed from ethylenically unsaturated monomers including a zwitterionic monomer having the general formula



in which Y is an ethylenically unsaturated group selected from the group consisting of $\text{H}_2\text{C}=\text{CR}-\text{CO}-\text{A}-$, $\text{H}_2\text{C}=\text{CR}-\text{C}_6\text{H}_4 \text{ A}^1-$, $\text{H}_2\text{C}=\text{CR}-\text{CH}_2\text{A}^2$, $\text{R}^2\text{O}-\text{COCR}=\text{CR}-\text{CO}-\text{O}$, $\text{RCH}=\text{CH}-\text{CO}-\text{O}-$, $\text{RCH}=\text{C}(\text{COOR}^2)\text{CH}_2-\text{CO}-\text{O}$,



A is -O- or NR¹;

A¹ is selected from the group consisting of a bond, (CH₂)_IA² and (CH₂)_I SO₃⁻ in which I is 1 to 12;

A² is selected from a bond, -O-, O-CO-, CO-O, CO-NR¹-, -NR¹-CO, O-CO-NR¹- and NR¹-CO-O-;

R is hydrogen or C₁₋₄ alkyl;

R¹ is hydrogen, C₁₋₄-alkyl or BX;

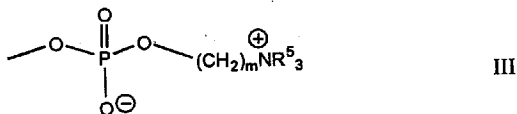
R² is hydrogen or C₁₋₄ alkyl;

B is selected from the group consisting of a bond, straight and branched alkanediyl groups, alkylene oxaalkylene groups, and alkylene (oligooxaalkylene) groups, optionally containing one or more fluorine substituents; and

X is a zwitterionic group.

41. (withdrawn): A process according to claim 40 in which X has the general formula

III



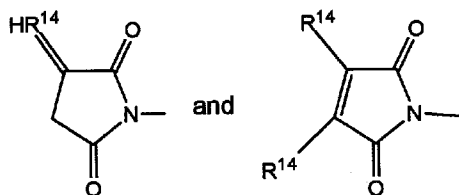
where the groups R⁵ are the same or different and each is hydrogen or C₁₋₄ alkyl, and m is from 1 to 4.

42. (withdrawn): A process according to claim 40 in which the zwitterionic monomer is 2-methacryloyloxyethyl-2'-trimethylammonium ethyl phosphate inner salt.

43. (withdrawn): A process according to claim 23 in which the ionic block is formed of ethylenically unsaturated monomers including an ionic monomer of general formula VI



in which Y^1 is selected from the group consisting of $H_2C=CR^{14}-CO-A^8-$, $H_2C=CR^{14}-C_6H_4-A^9-$, $H_2C=CR^{14}-CH_2A^{10}$, $R^{16}O-CO-CR^{14}=CR^{14}-CO-O$, $R^{14}CH=CH-CO-O-$, $R^{14}CH=C(COOR^{16})CH_2-CO-O$,



A^8 is $-O-$ or NR^{15} ;

A^9 is selected from the group consisting of a bond, $(CH_2)_qA^{10}$ and $(CH_2)_qSO_3-$ in which q is 1 to 12;

A^{10} is selected from the group consisting of a bond, $-O-$, $O-CO-$, $CO-O$, $CO-NR^{15}$, $-NR^{15}-CO$, $O-CO-NR^{15}$ and $NR^{15}-CO-O-$;

R^{14} is hydrogen or C_{1-4} alkyl;

R^{15} is hydrogen, C_{1-4} -alkyl or B^1Q ;

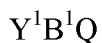
R^{16} is hydrogen or C_{1-4} alkyl;

B¹ is selected from the group consisting of a bond, straight and branched alkanediyl groups, alkylene oxaalkylene groups and alkylene (oligooxalkylene) groups, optionally containing one or more fluorine substituents; and

Q is an ionic or ionisable moiety.

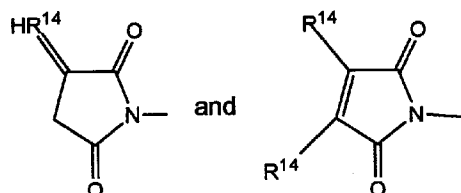
44. (withdrawn): A process according to claim 43 in which Q is selected from groups having the formula -NR¹⁷_p, -PR¹⁷_p and SR¹⁷_r, in which p is 2 or 3, r is 1 or 2, the groups R¹⁷ are the same or different and each is selected from the group consisting of hydrogen, C₁₋₂₄ alkyl and aryl, or two of the groups R¹⁷ together with the heteroatom to which they are attached from a 5 to 7 membered heterocyclic ring or three R¹⁷ groups together with the heteroatom to which they are attached form a 5 to 7 membered heteroaromatic ring, either of which rings may be fused to another 5 to 7 membered saturated or unsaturated ring, and any of the R¹⁷ groups may be substituted by amino or hydroxyl groups or halogen atoms.

45. (currently amended): A composition comprising a block copolymer having an overall ionic charge and associated with the polymer a biologically active compound having a charge opposite that of the polymer wherein the block copolymer comprises at least one zwitterionic block which has pendant zwitterionic groups and at least one ionic block which comprise ionic groups to confer said overall charge, wherein the biologically active compound is anionic and wherein the ionic block is formed of ethylenically unsaturated monomers including an ionic monomer of general formula VI:



VI

in which Y^1 is selected from the group consisting of $H_2C=CR^{14}-CO-A^8$ -, $H_2C=CR^{14}-C_6H_4-A^9$ -, $H_2C=CR^{14}-CH_2A^{10}$ -, $R^{16}O-CO-CR^{14}=CR^{14}-CO-O$ -, $R^{14}CH=CH-CO-O$ -, $R^{14}CH=C(COOR^{16})CH_2-CO-O$ -,



A^8 is $-O-$ or NR^{15} ;

A^9 is selected from the group consisting of a bond, $(CH_2)_qA^{10}$ and $(CH_2)_qSO_3-$ in which q is 1 to 12;

A^{10} is selected from the group consisting of a bond, $-O-$, $O-CO-$, $CO-O$, $CO-NR^{15}$ -, $-NR^{15}-CO$, $O-CO-NR^{15}$ -, and $NR^{15}-CO-O$;

R^{14} is hydrogen or C_{1-4} alkyl;

R^{15} is hydrogen, C_{1-4} alkyl or B^1Q ;

R^{16} is hydrogen or C_{1-4} alkyl;

B^1 is selected from the group consisting of a bond, straight and branched alkanediyl groups, alkylene oxaalkylene groups, and alkylene (oligooxalkylene) groups, optionally containing one or more fluorine substituents; and

Q is $-NR^{17}_2$ where each R^{17} is the same and is C_{1-12} alkyl,

wherein the biologically active compound and polymer are associated with one another in the form of particles.

REMARKS

Preliminary matters

Applicants wish to thank the Examiner for the courtesy extended during the personal Interview held on July 27, 2010. Applicants believe that the present amendment is in accordance with what was discussed during the Interview.

Amendment summary

Claims 1 and 45 are amended to recite that the biologically active compound and polymer are associated with one another in the form of particles. Support for this amendment may be found, e.g., in at least Claim 6.

No new matter is added by this Amendment, and Applicants respectfully submit that entry of this Amendment is proper.

Status of the claims

Claims 1-22, 28-35, and 45 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over Claims 1-43 of copending U.S. Application No. 10/542,333 in view of Storch et al. (WO 98/22517) (hereinafter “Storch”). Claims 1-22, 28-35, and 45 also stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over Claims 1, 33-78 of copending U.S. Application No. 10/501,393 in view of Storch. In addition, Claims 1-22, 28-35, and 45 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over Claims 29-50 of copending U.S. Application No. 10/544,113 in view of Storch. Further, Claims 1, 20, 21, 33, and 34 have been